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(54) Title: PROCESSES TO GENERATE SUBMICRON PARTICLES OF WATER-INSOLUBLE COMPOUNDS

(57) Abstract

Submicron particles of water-insoluble compounds, particularly drugs, are prepared by simultaneously stabilizing microparticulate suspensions of same with surface modifier molecules by rapid expansion into an aqueous medium from a compressed solution of the compound and surface modifiers in a liquefied gas and optionally homogenizing the aqueous suspension thus formed with a high pressure homogenizer.

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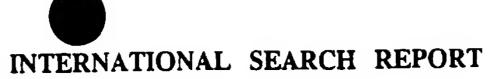
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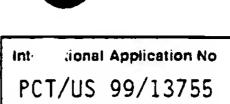


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C. DOCUM	ENTS CONSIDERED TO BE RELEVANT		
Category •	Citation of document, with indication, where appropriate, of the re-	levant passages	Relevant to claim No.
Ε	WO 99 52504 A (HOFFMANN LA ROCHE 21 October 1999 (1999-10-21) the whole document)	1–16
A	WO 97 14407 A (RES TRIANGLE PHARMACEUTICALS; UNIV TEXAS (US) HENRIKSEN INGE B (U) 24 April 1997 (1997-04-24) cited in the application the whole document	•	1-16
Α	WO 95 21688 A (WEIDNER ECKHARD ; ZELJKO (SI); NOVAK ZORAN (SI)) 17 August 1995 (1995-08-17)		
A	US 3 998 753 A (ANTOSHKIW THOMAS ET AL) 21 December 1976 (1976-12-		
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	Custon of document, with indication where appropriate of the minutes and		Relevant to claim No.
Category 5	Citation of document, with indication, where appropriate, of the relevant passages		поочан до стати но.
A	G. DONSI ET AL.: "POSSIBILITY OF APPLICATION TO PHARMACEUTICAL FIELD" PHARM. ACTA HELV,1991 - 1991, pages 170-173, XP002900588		
		•	



information on patent family members

Inte lonal Application No PCT/US 99/13755

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 9952504	Α	21-10-1999	NONE		
WO 9714407	Α	24-04-1997	AU AU EP	709262 B 7461796 A 0855906 A	26-08-1999 07-05-1997 05-08-1998
WO 9521688	A	17-08-1995	SI AT CA DE DK EP ES GR JP	9400079 A 159184 T 2182786 A 59500808 D 744992 T 0744992 A 2109095 T 3025495 T 9508851 T	31-10-1995 15-11-1997 17-08-1995 20-11-1997 02-06-1998 04-12-1996 01-01-1998 27-02-1998 09-09-1997
US 3998753	A	21-12-1976	AT AT BE DE FR GB IT JP NL	351912 B 625675 A 832331 A 2534091 A 2281961 A 1502895 A 1050722 B 51041732 A 7509586 A	27-08-1979 15-01-1979 12-02-1976 26-02-1976 12-03-1976 08-03-1978 20-03-1981 08-04-1976 17-02-1976